“Strawman” Priority Setting Process for Endocrine Disruptor Screening and Testing

January 20, 1999

Background

The Endocrine Disruptor Screening and Testing Program has five major components:

1. Sorting, in which chemicals are classified according to the availability of information on each chemical's endocrine-disrupting potential.

2. Priority setting, in which EPA will determine the priority order for entry into Tier 1 screening (T1S).

3. Tier 1 screening, a battery of in vitro and in vivo assays designed to identify those chemicals that are not likely to interact with the estrogen, androgen, or thyroid hormone systems (EAT).

4. Tier 2 testing, a battery of assays designed to determine whether a chemical may have an effect in humans, fish or wildlife similar to that of naturally occurring hormones and to identify, characterize, and quantify those effects for EAT effects.

5. Hazard assessment, a weight-of-evidence evaluation of Tier 1 and Tier 2 results.

It is expected that the sorting will result in a relatively small number of chemicals proceeding directly to Tier 2 testing or hazard assessment and that the vast majority of chemicals will be placed in priority setting for Tier 1 screening.

EPA proposes that all chemicals would initially be subject to priority setting for T1S except for chemicals with sufficient data to go directly to tier 2 testing or hazard assessment or for the polymers and some exempted chemicals as described in the Endocrine Disruptor Screening Program Proposed Statement of Policy published in the federal register on December 28, 1998.

Prioritizing Chemicals for Endocrine Disruptor Tier 1 Screening

The Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC) stated that the priority setting system for T1S should be transparent, reflect the guiding principles below for weighting data, and rely heavily, but not exclusively, on empirical data to set priorities.

The guiding principles are that more weight should be given to biological data relevant to large populations, disproportionately exposed populations, or susceptible populations. More weight should be given to chemicals likely to be internalized by an organism and more weight should be given to releases that are likely to lead to exposure. The EDSTAC also stated their

belief that production volume should not be used to rank industrial chemicals relative to pesticides.

The EDSTAC felt that empirical data showing chemicals found in organisms should be weighted heavily, that empirical evidence of effects should be weighted more heavily than models, and that existing empirical data could be used to improve the predictive capability of models.

The EDSTAC recommended a "compartment-based priority setting strategy" that builds upon distinct exposure- and effects-related information categories and criteria as well as a category of specially targeted priorities. The reason this approach was recommended over approaches that strive to develop a single rank-ordered priority list that integrates all exposure- and effects-related categories and criteria was the EDSTAC felt that the available data was very different from one chemical to another. Using a compartment-based approach, chemicals with similar data are compared against each other. The compartment based approach also helps to avoid being totally driven by the "looking under the lamp post" phenomenon.

The EDSTAC listed the following categories and subcategories of information that should be considered in developing the compartment-based approach.

A. Exposure-Related Information

1. Biological sampling data
2. Environmental, occupational, consumer product, and food-related data (sampling and/or use data)
3. Environmental releases
4. Production volume
5. Fate and transport data and models

B. Effects-Related Information

1. Toxicological laboratory studies and databases
2. Epidemiologic and field studies and databases
3. Predictive biological activity or effects models (e.g. SAR, QSAR)
4. Results of high throughput pre-screening

C. Integrated Effects and Exposure Information

D. Specially Targeted Priorities

1. Mixtures
2. Naturally Occurring Non-Steroidal Estrogens
3. Nominations

The EDSTAC did not reach agreement on the definition or weighting of specific compartments. Following the basic framework and guiding principles laid out in the EDSTAC report, EPA has developed an initial "strawman" proposal for a compartment-based system.

Proposed Approach

In the proposed approach EPA uses the four categories proposed by the EDSTAC (i.e. specially targeted priorities, exposure-related information, effects-related information, and an integrated effects and exposure information category). Compartments will be defined for each of these categories. It is assumed that a database will be developed to contain the rank-ordered lists of chemicals within each compartment as well as the weights and algorithm to select chemicals for entry into tier 1 screening. It is also assumed that selection of chemicals for T1S will occur in phases.

EPA will need to determine how many chemicals to select in total for the first phase of the screening and testing process (at this time that determination has not yet been made). The EDSTAC felt that the total number of chemicals selected could have ramifications for the weights and/or for the number of compartments. For example they stated in their report that if the total number selected is relatively small, this could lead to having fewer compartments since relatively few chemicals would be selected from each compartment.

In developing the strawman proposal, EPA adopted the following working definition of a compartment:

All chemicals within a compartment share the feature(s) that define the compartment (e.g. chemicals with TRI release data). The defining feature(s) of the compartment should, if possible, be suitable for sorting chemicals within the compartment into a rank-ordered list.

The table below summarizes the "strawman" proposal. The table has the four categories and multiple compartments under each category (except for the integrated effects and exposure category). In order to select chemicals for screening, the following steps are required:

1. Define the compartments
2. Rank order chemicals within each compartment
3. Assign percentage weights to each compartment with all of the weights summing to 100%
4. Based upon the number of chemicals to be screened in phase I, use the weights and rank-ordered lists of chemicals to select chemicals from each compartment.
5. As needed, review the chemicals selected from each compartment to ensure that obviously incorrect selections are not made (e.g. a chemical ranked high for persistence by the proposed modeling approach that in reality undergoes rapid hydrolysis).
6. Select and propose the list of phase I chemicals for entry into T1S screening. (Note: The proposal of this list does not constitute the making of "findings" for rule making purposes.)

As stated above, in the proposed approach there are four categories of chemicals and multiple compartments within each category.

Specially Targeted Priorities

The first category, specially targeted priorities, is different from the others in that some very specific recommendations were made by EDSTAC about chemicals to be screened or about specific chemicals or mixtures which should be screened. There are three compartments in this category.

Exposure-Related Information

The second category is the exposure-related information category. There are twelve compartments in the exposure category. The compartments in this category contain information relevant to predicting the likelihood of exposure to humans or to wildlife. The compartment containing chemicals found in biological monitoring data may predict exposure with a relatively high degree of reliability. Exposure is also likely to chemicals in food and drinking water, chemicals in consumer/cosmetic products, and chemicals for which occupational exposure standards have been developed. Exposure is also likely but perhaps less so for chemicals found in environmental monitoring data. Exposure related information such as persistence in the environment, bioaccumulation potential, release to the environment, and production volume give an indirect indication of the likelihood of exposure.

Possible approaches to rank ordering lists of chemicals within compartments include looking at the frequency of occurrence of chemicals in biological and environmental monitoring studies, frequency of occurrence within drinking water and food monitoring studies, and frequency of occurrence within consumer and cosmetic products. Alternatively, it may be possible to use frequency of occurrence in combination with some sort of normalized concentration or intake estimates to rank-order chemicals within some of these compartments. This approach would allow the use of additional information (i.e. concentration data) in establishing the rank-ordered lists. A compartment consisting of chemicals with occupational exposure standards may be rank-ordered by the numerical value of those exposure standards. Chemicals in compartments based on persistence in the environment may be rank-ordered by half-life which may be predicted based upon measured or predicted physical-chemical properties and fate along with the use of multimedia models. Likewise, bioaccumulation potential may be estimated based upon estimated or measured physical-chemical properties and models. Chemicals in compartments based on release to the environment and production volume may be rank-ordered respectively by mass released and mass produced.

Effects-Related Information

The third category is the effects-related information category. There are seven compartments in the effects category. The compartments in this category contain information relevant to predicting the likelihood that the chemical can cause effects due to endocrine disruption. When they are available, epidemiological and clinical data on chemicals showing endocrine target organ effects in humans are relatively strong indicators of potential endocrine

disruptor effects in people. Studies using laboratory animals on reproductive or developmental toxicity, carcinogenic effects in endocrine target tissues, and subchronic studies on effects in endocrine target tissues may also be good indicators of a chemical's potential to be an endocrine disruptor in humans. In vitro studies such as the HTPS assays, and QSARs may also provide useful information for screening chemicals for their endocrine disruption potential in humans. For fish and aquatic invertebrates as well as mammalian and avian wildlife, studies showing reproductive, growth and behavior effects provide useful information for screening a chemical's endocrine disruptor effects in these species. When data is not available, QSARs may in some cases be useful here too.

Possible approaches to rank-ordering chemicals within the effects compartments include ranking on a numerical scale where the data allow it (e.g. NOAEL and LOAEL data, HTPS data, QSARs). In some cases all the data may allow is a positive or negative indication, in which rank ordering would not be possible.

Integrated Effects and Exposure Information

In this "strawman", we have not proposed any approaches for combining exposure and effects into compartments in the integrated exposure and effects category. We are interested in ideas on how we might do this. We are also interested in ideas about how we might deal with chemicals that appear in multiple compartments (e.g. include a multi-hit compartment or, use multiple hits as part of the rank ordering for those compartments that have a lot of ties?)

Hypothetical Example

As a hypothetical example of a compartment-based priority setting approach, suppose a priority setting system consisted of three compartments, each of which contained chemicals in a rank-ordered list. Furthermore, assume that the compartment #1 contained 100 chemicals, compartment #2 contained 1000 chemicals, and compartment #3 contained 10,000 chemicals. Assume that each compartment is given a equal weight of 33.3%. If a total of 99 chemicals were to be selected, this means that 33 chemicals will be selected from each of the three compartments. So, for compartment #1, the 33 highest ranked chemicals out of the 100 chemicals in compartment#1 will be selected. For compartment #2, the 33 highest ranked chemicals out of the 1000 in compartment#2 will be selected. And finally for compartment #3, the 33 highest ranked chemicals out of the 10,000 chemicals in compartment#3 will be selected.

Proposed Compartments for EDSP Priority Setting

<table>
<tr><th>Specially Targeted Priorities</th><th>Exposure</th><th>Effects</th><th>Exposure & Effects</th></tr>
<tr><td>Nominations</td><td>Human Biological Monitoring Data</td><td>Epidemiological and clinical data on endocrine target organ effects.</td><td rowspan="11"></td></tr>
<tr><td>EDSTAC Recommended Mixtures</td><td>Ecological Biological Monitoring Data</td><td>Reproductive/developmental toxicity - NOAELs/LOAELs from studies in laboratory animals.</td></tr>
<tr><td rowspan="9">EDSTAC Recommended NONES</td><td>Chemicals in food and drinking water</td><td>Carcinogenicity - positive/negative results in endocrine target tissues</td></tr>
<tr><td>Chemicals in consumer and cosmetic products</td><td>Subchronic toxicity - NOAELs/LOAELs for endocrine targets</td></tr>
<tr><td>Occupational exposure chemicals</td><td>High Throughput Pre- Screen test results (degree of receptor binding)</td></tr>
<tr><td>Monitoring data Surface and ground water</td><td>Ecotoxicity - field and laboratory studies</td></tr>
<tr><td>Monitoring data Indoor and outdoor air</td><td rowspan="6">Quantitative Structure-Activity Relationships (QSARs) for estrogen receptor binding</td></tr>
<tr><td>Monitoring data Sediments/soil</td></tr>
<tr><td>Persistence</td></tr>
<tr><td>Bioaccumulation potential</td></tr>
<tr><td>Environmental releases</td></tr>
<tr><td>Production and import volumes</td></tr>
</table>

Below are definitions of the specially targeted priority compartments and a series of one page descriptions of the exposure and effects compartments. The one page descriptions include a

definition of the compartment, a listing of relevant data bases, an estimate of the number of chemicals in each compartment (where it was possible to estimate at this stage of the project) and possible options for rank-ordering chemicals within each compartment.

Definitions of the Specially Targeted Priority Compartments

Nominations: Chemical substances or mixtures nominated by citizens who are disproportionately exposed because of the group or community to which they belong, or because an ecosystem is disproportionately exposed.

EDSTAC Recommended Mixtures: The EDSTAC recommended that representative samples of six types of mixtures be screened and tested. The six types of mixtures are contaminants in human breast milk, phytoestrogens in soy-based infant formulas, mixtures of chemical substances most commonly found at hazardous waste sites, pesticide fertilizer mixtures found in surface water and groundwater, drinking water disinfection byproducts, and gasoline.

EDSTAC Recommended Naturally Occurring Non-Steroidal Estrogens (NONEs): The EDSTAC recommended that representative NONEs be screened and tested. These representative NONEs are:
1) Isoflavones: genistein, daidzein, miroestrol, bichanin A, formononetin, equol;
2) Flavanones: kaemferol, naringenin;
3) Coumestans: coumesterol;
4) Dihydrochalcones: phoretin;
5) Triterpenes: betulafolienetriol (ginseng);
6) Lignans: enterolactone; and
7) Beta-resorcyclic lactones: zearalenone, zearalenol, zearanol

Definitions of Exposure Compartments

Name of compartment

Human Biological Monitoring Data

Definition of compartment

The chemicals in this compartment have all been found in humans in monitoring studies

Relevant databases and tools

The Third National Health and Nutrition Examination Survey (NHANES III) conducted by the Center for Health Statistics/Centers for Disease Control and Prevention.

The National Human Adipose Tissue Survey conducted by the National Human Monitoring Program of the Office of Pollution Prevention and Toxics/ United States Environmental Protection Agency.

The National Human Exposure Assessment Survey (NHEXAS), conducted by EPA's Office or Research and Development monitored chemicals in blood and urine (this data is currently being evaluated).

Approximate number of chemicals in the compartment

NHANES III measured 39 "priority toxicants" which included VOCs, pesticides and metabolites in blood.

NHATS targeted 111 semivolatile organic chemicals (including some pesticides) in the 1986 chemical analysis of human adipose tissue.

NHEXAS had 56 target analytes that included pesticides, VOCs and metals.

Potential options for ranking within compartment

Rank chemicals by frequency of occurrence in human biological samples.

Alternatively, rank chemicals by body burden assuming a "standard human body" and using measured concentration data from adipose tissue and blood.

Name of Compartment

Ecological Biological Monitoring Data

Definition of compartment

Ecological biological monitoring involves the sampling of a wide range of species and sample matrices for exposure to environmental contaminants

Relevant databases and tools

The new Storage and Retrieval System(STORET) combines information from the STORET Water Quality System(WQS) with that of the Biological Information System(BIOS) and the Ocean Data Evaluation System(ODES).

Environmental Contaminant Data Management System which contains compilations of analytical data of 100,000 samples of invertebrates, fish and wildlife.

Great Lakes Fish Monitoring Program contains a compilation of data from a 30-year biomonitoring effort conducted by the Great Lakes Science Center of the U.S. Geological Survey.

TSCATS 2.0 database which tracks the existence (but not the values) of environmental monitoring data from TSCA submissions. This database, in the process of development, contains data that used to be available in the OPPT CECATS database.

Approximate number of chemicals in the compartment

TSCATS 2.0 has about 8000 chemicals.

STORET houses approximately 25 million sample records and about 150 million analysis records. The number of chemicals in STORET is unknown at this time. The utility of STORET to this prioritization effort may be limited due to uncertainty about the quality of the data and the difficulty of extracting it in a suitable form.

The Environmental Contaminant Data Management System contains about 625 compounds.

Great Lakes Fish Monitoring Program contains over 550 compounds. Total number of compounds for this compartment, estimated assuming the numbers supplied above are close to actual numbers, could be anywhere from 700- 1100 on up.

Potential Options for Ranking Within Compartment

Rank by frequency of appearance in biological tissues.

Name of compartment

Chemicals in food and drinking water

Definition of compartment

Direct and indirect food additives, contaminants found in food and drinking water

Relevant databases and tools

FDA lists of direct and indirect food additives; food inspection data from FDA and USDA; drinking water monitoring data from EPA (Safe Drinking Water Information System (SDWIS)). SDWIS has data on frequency of occurrence, concentrations found, and size of the population served by the tested water systems.

Approximate number of chemicals in the compartment

FDA has approved over 3000 direct food additives and over 2500 indirect food additives. EPA has drinking water monitoring data on about 100 chemicals. Total number of chemicals in compartment (taking into account overlaps) is probably about 5000-6000.

Potential options for ranking within compartment

1. Rank by frequency of use/occurrence in food or water.
2. Rank by concentrations found in food or water.
3. Rank by number of persons exposed.

Name of compartment

Chemicals in consumer and cosmetic products

Definition of compartment

Chemicals intentionally added or known to be emitted from consumer and cosmetic products

Relevant databases and tools

FDA's database from its Cosmetic Voluntary Registration Program lists the number of products that contain each chemical. EPA's Source Ranking Database (SRD) has information on chemicals used in or emitted from a wide range of consumer products. The SRD has product-specific information on the chemicals used and their concentrations in each product.

Approximate number of chemicals in the compartment

FDA's database contains about 2400 cosmetic ingredients. EPA's Source Ranking Database (SRD) contains about 1400 chemicals. Total number of chemicals in compartment (taking into account overlaps) is probably about 2500-3500.

Potential options for ranking within compartment

1.Rank by frequency of use (number of products containing chemical)

2.Option(s) for including amount of chemical used in the ranking? (The SRD includes formulation data that could allow this. Is there similar data readily available for cosmetic products?)

Name of compartment

Occupational Exposure Chemicals

Definition of compartment

This compartment consists of a list of chemicals that have occupational exposure limits. It is assumed that for the most part, there is the potential for widespread occupational exposure to chemicals for which occupational limits have been developed.

Relevant databases and tools

OSHA Permissible Exposure Limits (PELs)

NIOSH Recommended Exposure Limits (RELs)

ACGIH Threshold Limit Values (TLVs)

(Alternatively, if a database(s) of readily available, and representative, monitoring data were identified, those monitoring data might be substituted for the PELs/RELs/TLVs as a measure of potential exposure. Perhaps the OSHA Inspection Database could be used for this purpose.)

Approximate number of chemicals in the compartment

About 600 chemicals have PELs and or RELs

About 700 chemicals have TLVs

Since there is probably a lot of overlap, the total number of chemicals is probably around 700.

Potential options for ranking within the compartment

The list of chemicals may be rank-ordered by the highest of their PEL, REL, or TLV values. Chemicals with the highest values in the rank-ordered list may have the highest exposure.

Name of compartment

Environmental monitoring data - Surface and ground water

Definition of compartment

Chemicals monitored in surface and ground waters of the United States

Relevant databases and tools

USGS has the National Water Quality Assessment (NAWQA) program, the Toxic Substances Hydrology Program (TSHP) and the National Stream Quality Accounting Network (NASQAN).

The Water Quality System, the largest subset of the STORET database utility operated by EPA, includes measurements of the chemical composition of sampled waters.

EPA's Office of Pesticide Programs has two databases on the occurrence of pesticides in groundwater—the National Pesticide Survey and the Pesticides in Groundwater Database. The Survey looked for 126 pesticides (101 parent and 25 degradates); the Groundwater Database searched for 302 pesticides and detected 132.

Approximate number of chemicals in the compartment

There are approximately 270 chemicals in the USGS database. Of these 84 are pesticides.

STORET houses approximately 25 million sample records and about 150 million analysis records. The number of chemicals in STORET is unknown at this time. The utility of STORET to this prioritization effort may be limited due to uncertainty about the quality of the data and the difficulty of extracting it in a suitable form.

Potential options for ranking within compartment

Chemical concentration, frequency of observation

Name of compartment

Environmental monitoring data - Indoor and outdoor air

Definition of compartment

Chemicals monitored in indoor and outdoor air of the United States

Relevant databases and tools

EPA's Office of Air maintains the Aerometric Information Retrieval System, which contains the Air Quality Subsystem (AQS) database. The AQS contains either one-hour or 24-hour averages of pollutant concentrations from thousands of monitoring stations. Number of different chemicals monitored is not known.

The following sources were cited in a recent EPA-ORD report:

Shah and Singh, *ES&T*, **2**(12): 1381-1388, 1988. A literature survey with outdoor concentrations of U.S. ambient air data through 1986.

Kelly et al., *ES&T*, **28**(8): 378A-387A, 1994. A comprehensive update of Shah and Singh, 1988.

Samfield, EPA-600-R-92-025 (NTIS PB92-158468), 1992. Literature survey of U.S. and foreign indoor concentrations through the late 1980's from residences, office buildings, schools, other commercial buildings.

Brown et al., *Indoor Air*, **4**:123-134, 1994. Comprehensive compilation and analysis of U.S. and European literature, with data on residences, office buildings, schools and other buildings. Includes indoor concentrations and indoor/outdoor ratios.

NOPES Final Report, EPA/600/3-90/003 (NTIS PB90-152224), January 1990. The Nonoccupational Pesticide Exposure Study is an EPA field study with indoor and outdoor concentrations and I/O ratios from 350 samples taken in homes in Jacksonville, FL and Chicopee-Springfield, MA.

Sheldon et al., "Indoor Pollutant Concentrations and Exposures", California Air Resources Board, contract A833-156, final report, January 1992. A field study of indoor and outdoor concentrations and I/O ratios from 128 homes in Woodland, CA.

Daisey et al., *Atm. Environ*. **28**(22):3557-3562, 1994. A field study of indoor and outdoor concentrations and I/O ratios from 12 office buildings in northern CA with 3 different types of ventilation systems.

Shields, Fleischer, and Weschler, *Indoor Air*, **6**:2-17, 1996. Afield study of indoor and outdoor concentrations and I/o ratios from 70 telephone company buildings in 25 states and Washington DC., 50 telecommunications centers, 11 office buildings, and 9 data centers.

Other sources:

The National Human Exposure Assessment Survey (NHEXAS) will include VOCs in indoor air in three different regions in the U.S.

Approximate number of chemicals in the compartment

in the low hundreds?

Potential options for ranking within compartment

Chemical concentration, frequency of observation

Name of compartment

Environmental Monitoring Data- Sediments/soil

Definition of compartment

Monitoring data for chemical contaminants found in sediments and soil

Relevant databases and tools

The National Sediment Inventory contains data on sediment/soil testing, toxicity and tissue residues from studies conducted from 1980-93.

The Water Quality System, the largest subset of the STORET database utility operated by EPA, includes measurements of the chemical composition of sampled waters and sediments.

The Superfund Contract Lab Program (CLP) database for data on chemicals in soil.

Other possible relevant databases include Environmental Monitoring and Assessment Program, National Estuary Program and Chesapeake Bay Monitoring Program.

Approximate number of chemicals in the compartment

The number of chemicals in the National Sediments Inventory is unknown at this time.

STORET houses approximately 25 million sample records and about 150 million analysis records. The number of chemicals in STORET is unknown at this time. The utility of STORET to this prioritization effort may be limited due to uncertainty about the quality of the data and the difficulty of extracting it in a suitable form.

The number of chemicals in the CLP database is probably in the thousands.

Potential options for ranking within compartment

Rank by frequency of appearance and abundance in sediments/soil.

Name of compartment

Persistence

Definition of compartment

This compartment consists of a list of chemicals that has been rank-ordered by estimated environmental persistence. It is important to distinguish between ability to persist in a given medium (air, water, soil, sediment) and overall persistence. A chemical substance may be transformed to other molecular species, but it may also partition from one medium to another. Persistence in the environment as a whole is a distinct concept that is based on the observations that the environment behaves as a set of interconnected media, and that a chemical substance released to the environment will become distributed in these media in accordance with its intrinsic (physical/chemical) properties and reactivity. Multimedia models are required to assess "overall persistence".

Relevant databases and tools

The Syracuse Research Corporation (SRC) PHYSPROP database
The SRC Environmental Fate Data Base (EFDB)
The SRC Estimation Programs Interface (EPI)(chemical property estimation software)
The Equilibrium Quality Criterion (EQC) model (multimedia modeling software)
The Handbook of Environmental Degradation Rates (Lewis Publishers: Boca Raton, FL)

Approximate number of chemicals in the compartment

The SRC SMILECAS file has approx. 103,000 entries. The chemicals in this file are the discrete organics. The list was originally started using the TSCA Inventory and adding additional chemicals.

Potential options for ranking within the compartment

A key question for all options listed below is how the required half-lives will be obtained. The number of measured values available is very limited.

1. Rank using a multimedia fate model such as the EQC or equivalent model, preferably run under equilibrium, steady-state conditions with consideration of reaction half-lives (i.e., level III). Such models yield an "overall persistence" number that can be used for the rank ordering.

2. Rank by reaction half-life; e.g., biodegradability as reflected by experimental data and/or predicted by estimation methods such as the BIOWIN program in EPI.

3. Rank by persistence in a specific medium; e.g., half-life for dissipation (disappearance) of the chemical in soil.

Name of compartment

Bioaccumulation potential

Definition of compartment

A list of chemicals containing the discrete organics as well as some inorganic substances (metals), ranked by bioaccumulation potential.

Relevant databases and tools

The Syracuse Research Corporation (SRC) ISISBCF file
The SRC Estimation Programs Interface (EPI)(chemical property estimation software)
The Aquatic Information Retrieval (AQUIRE) database
The compilation of bioaccumulation and biodegradation data published by the Japanese Chemicals Inspection and Testing Institute (CITI)

Approximate number of chemicals in the compartment

The SRC SMILECAS file has approx. 103,000 entries. The chemicals in this file are the discrete organics. The list was originally started using the TSCA Inventory and adding additional chemicals.

Potential options for ranking within the compartment

A key question for all options listed below is how the required bioaccumulation information will be obtained. The number of measured values available is very limited.

1. Rank using measured (preferred) or estimated BCF values. First consult the ISISBCF file for measured values; then use the BCFWIN program in EPI to estimate BCF for the remaining (majority of) chemicals. ISISBCF already includes data in other common sources such as the AQUIRE and CITI databases.

2. Rank using measured (preferred) or estimated octanol/water partition coefficients (K_{ow}). K_{ow} values are available for a vastly greater number of chemicals (thousands) than is the case for measured BCFs.

3. Develop some hybrid approach, perhaps involving a hierarchy of sources of measured bioaccumulation factors (BAFs)(preferred) and BCFs.

Name of compartment

Environmental releases

Definition of compartment

The chemicals in this compartment are all TRI chemicals.

Relevant databases and tools

The most current version of the Toxic Release Inventory Database (1997 releases).

Approximate number of chemicals in the compartment

The current TRI chemical list contains 579 individually listed chemicals and 28 chemical categories (including 2 delimited categories containing 39 chemicals). Note: Three chemicals on the current list (methyl mercaptan, hydrogen sulfide, and 2,2-dibromo-3-nitrilopropionamide) are under administrative stays and are not currently reportable.

Potential options for ranking within compartment

The Toxics Release Inventory Database has information for each listed chemical and each reporting facility for onsite releases to air, water, and land (e.g. landfill, land treatment, surface impoundment) as well as offsite transfers to POTWs and other treatment facilities. This information may be used to rank-order the chemicals in the releases compartment. Options include:

1. Rank-order by sum of environmental releases and transfers
2. Rank-order by sum of environmental releases

Name of compartment

Annual chemical production/import volume

Definition of compartment

Total U.S. production and/or import volume of chemical, expressed in mass units per year, e.g., pounds or kilograms

Relevant databases and tools

Production data for chemicals on the TSCA Inventory have been updated through the Inventory Update Rule (IUR) in 1986, 1990, 1994, and 1998. Data from the 1998 IUR have just been received by the Agency and are not yet available for use. The Chemical Update System (CUS) database contains the data reported under the IUR. The SIS/L database on EPA-OPPT's Local Area Network has non-confidential production volume information in its CUS94 Production and US High Volume lists. The CUS94 list is of chemicals with greater than 10,000 lbs. production reported under the 1994 Inventory Update Rule (IUR). The US High Volume list is those discrete organic chemicals with production greater than one million lbs. on the 1990 IUR.

Approximate number of chemicals in compartment

More than 12,000 discrete organic chemicals have been reported on one or more IURs. It is estimated that another 2000-3000 inorganics and other IUR-exempt chemicals are produced in excess of the 10,000 lb IUR reporting threshold, bringing the total number of chemicals produced in quantities above 10,000 lb to about 15,000. The CUS1990 lists over 2800 chemicals produced in quantities over one million lb. Accounting for inorganics and other IUR-exempt chemicals, a total of 3000-4000 chemicals are estimated to be produced in quantities over one million lb. Over 300 of these high-volume chemicals are produced in quantities exceeding one billion lb. Of the approximately 75,000 chemicals on the TSCA Inventory, about 50,000 eligible chemicals have never been reported on the IUR. It is assumed that these chemicals are either out of production or are produced in quantities under the 10,000 lb reporting threshold.

Potential options for ranking within compartment

Production volume amount

Definition of Effects Compartments

Name of compartment

Epidemiology and clinical data

Definition of compartment

Endocrine target organ effects in humans

Relevant databases and tools

Integrated Risk Information System (IRIS)
TSCA Chemical Assessment Tracking System (TSCATS)
EPA Office of Pesticide Programs data bases
Hazardous Substances Data Bank (HSDB)
Chemical Carcinogenesis Research Information System (CCRIS)
Registry of Toxic Effects of Chemical Substances (RTECS)

Approximate number of chemicals in the compartment

Estimated by OPPT to be up to 100

Potential options for ranking within compartment

Presence or absence of endocrine target organ effects

Name of compartment

Reproductive and developmental toxicity

Definition of compartment

Reproductive or developmental toxicity studies in laboratory animals (and in vitro systems)

Relevant databases and tools

Integrated Risk Information System (IRIS)
TSCA Chemical Assessment Tracking System (TSCATS)
EPA Office of Pesticide Programs databases
Hazardous Substances Data Bank (HSDB)
Registry of Toxic Effects of Chemical Substances (RTECS)
Developmental and Reproductive Toxicity (DART) Database

Approximate number of chemicals in the compartment

As of October, 1998, there were 143,831 entries in the RTECS data base. There were 6,047 chemicals with reproductive effects entries.

Potential options for ranking within compartment

NOAELs, and LOAELs if NOAELs are unavailable; positive/negative effects in vitro

Name of compartment

Carcinogenicity

Definition of compartment

Carcinogenic effects in endocrine target organ tissues, e.g., thyroid, pituitary and Leydig cell

Relevant databases and tools

Integrated Risk Information System (IRIS)
TSCA Chemical Assessment Tracking System (TSCATS)
EPA Office of Pesticide Programs data bases
Hazardous Substances Data Bank (HSDB)
Chemical Carcinogenesis Research Information System (CCRIS)
Registry of Toxic Effects of Chemical Substances (RTECS)

Approximate number of chemicals in the compartment

100 based on the number of studies with endocrine target organ effects according to Handbook of Carcinogenic pathways... ed. Gold & Zeiger.

Potential options for ranking within compartment

Positive or negative results in carcinogenesis bioassays. Evidence for an endocrine mechanism would be strengthened by negative genotoxicity indicators.

Name of compartment

Subchronic Toxicity

Definition of compartment

Effects in endocrine target tissues in laboratory animals

Relevant databases and tools

Integrated Risk Information System (IRIS)
TSCA Chemical Assessment Tracking System (TSCATS)
EPA Office of Pesticide Programs data bases
Hazardous Substances Data Bank (HSDB)
Registry of Toxic Effects of Chemical Substances (RTECS)
Priority Assessment of Food Additives (PAFA) Database

Approximate number of chemicals in the compartment

As of October, 1998, there were 143,831 entries in the RTECS data base. There were 1,752 chemicals with entries for multiple dose toxicity..

Potential options for ranking within compartment

NOAELs and LOAELs if NOELs are unavailable

Name of compartment

High Throughput Screen (HTPS)

Definition of compartment

Results from the HTPS battery of tests to measure receptor binding affinity potential

Relevant databases and tools

None. HTPS test results would be the content of this compartment

Approximate number of chemicals in the compartment

15,000

Potential options for ranking within compartment

Degree of receptor binding

Name of compartment

Quantitative structure-activity relationships (QSARs) for endocrine receptor binding

Definition of compartment

Modeled estimates of estrogen and other endocrine organ receptor binding affinity potential. (If available, QSARs for endocrine effects and gene activation could also be included.)

Relevant databases and tools

None. Estrogen and androgen receptor models would be used.

Approximate number of chemicals in the compartment

Unknown

Potential options for ranking within compartment

Degree of receptor binding

Name of compartment

Ecotoxicity

Definition of compartment

Reproductive, growth and behavior effects in fish and aquatic invertebrates, as well as in mammalian and avian wildlife.

Relevant databases and tools

ECOTOX Database
Aquatic Information Retrieval Data Base (AQUIRE)
Terrestrial Toxicity Data Base (TERRETOX)
TSCA Chemical Assessment Tracking System (TSCATS)
EPA Office of Pesticide Programs data bases
Ecotoxicity Structure-Activity Relationships Data Base (ECOSAR)
Assessment Tool for Ecological Risk (ASTER)

Approximate number of chemicals in the compartment

Unknown. There are 6,100 chemicals in the AQUIRE data base. The number of chemicals with studies on reproductive, growth and behavioral effects is a subset of 6,100.

Potential options for ranking within compartment

Highest ranking for adverse effects on natural populations; EC50, NOAEC and LOAEC values would be ranked over ECOSAR or ASTER predictions.